

# Mediastinal Staging in Non–Small Cell Lung Cancer



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## KEYWORDS

- Lung cancer staging • Mediastinal lymph nodes • Mediastinoscopy
- Endobronchial ultrasound

## KEY POINTS

- In the absence of distant metastases, lung cancer treatment is determined by the results of mediastinal lymph node staging.
- Occult mediastinal lymph node metastases can be missed by radiologic and needle-based staging methods.
- Aggressive staging of mediastinal lymph nodes improves staging accuracy.
- Improved accuracy of mediastinal lymph node staging results in more appropriate lung cancer treatment.
- Improved accuracy of mediastinal lymph node staging can improve stage-specific survival from lung cancer.

## IMPORTANCE OF PRETREATMENT STAGING IN THE MANAGEMENT OF NON–SMALL CELL LUNG CANCER

Despite advances in the treatment of non–small cell lung cancer, overall cure rates remain low. Only a relatively small proportion of patients with non–small cell lung cancer is diagnosed at an early stage; most are diagnosed only after there has been spread beyond the lung.<sup>1</sup> The optimal treatment of non–small cell lung cancer is stage specific.<sup>2</sup> Aggressive pretreatment staging efforts often lead to “upstaging,” which, in turn, results in improved stage-specific survival.<sup>3</sup>

In staging patients with non–small cell lung cancer, the initial goal is to rule out distant metastatic disease. For practical reasons, this is accomplished primarily via imaging studies. As a rule, these include whole-body PET/computed tomography (CT) as well as brain MRI scans. Typically, suspected sites of distant metastatic disease may be confirmed using image-guided percutaneous needle biopsy techniques.

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After excluding distant metastatic disease in the most feasible way, it is critical to rule out regional spread of tumor to the mediastinum. It has long been known that involvement of mediastinal lymph nodes greatly decreases the likelihood of cure using local treatment modalities (eg, radiotherapy or surgical resection) alone. The presence of mediastinal lymph node metastases makes control of systemic disease the priority, and chemoradiotherapy the mainstay of treatment, relegating surgical resection or stereotactic radiosurgical ablation to “adjuvant” treatment status.

### THE TIMING OF MEDIASTINAL LYMPH NODE STAGING

By definition, in non–small cell lung cancer, involvement of mediastinal lymph nodes with metastatic tumor is considered stage III and is associated with a worsened prognosis. In the absence of local symptoms, the focus of treatment for stage III non–small cell lung cancer shifts from local control of the primary tumor to systemic control, that is, the successful eradication of suspected occult micrometastatic disease. The addition of effective locoregional disease control may result in cure.

In patients with mediastinal lymph node involvement, surgical resection of non–small cell lung cancer is unlikely to result in a cure.<sup>4</sup> Preferred treatment involves the use of systemic chemotherapy as well as external beam radiotherapy to the primary tumor and involved mediastinal nodes. Although chemotherapy and radiotherapy are more easily tolerated when used sequentially, concurrent chemoradiotherapy results in improved patient outcomes with a greater likelihood of cure.<sup>5</sup> Survival of patients in whom unexpected mediastinal lymph node involvement is discovered at the time of surgical resection is somewhat improved with the addition of postoperative radiotherapy and chemotherapy.<sup>6</sup>

In selected patients, the addition of adjuvant surgical resection following chemoradiotherapy for stage III non–small cell lung cancer has resulted in improved survival and higher cure rates. The highest rates of cure in mediastinal lymph node–positive stage III non–small cell lung cancer are observed in patients who undergo surgical resection following preoperative concurrent chemoradiotherapy and who are found to have achieved effective eradication of metastatic tumor from their mediastinal lymph nodes<sup>7</sup> and a pathologic complete response of their primary tumor to preoperative chemoradiotherapy.<sup>8</sup>

For medically fit patients with stage III non–small cell lung cancer with mediastinal lymph node involvement, survival is maximized by trimodality therapy that combines chemotherapy, locoregional radiotherapy, and surgical resection.<sup>9</sup> Although postoperative radiotherapy improves the prognosis of patients whose mediastinal lymph node involvement is discovered unexpectedly at the time of surgical resection,<sup>6</sup> the chance of cure is highest in patients who undergo surgical resection following successfully “downstaging” with preoperative/neoadjuvant chemoradiotherapy. Patients who are not successfully “downstaged” by preoperative/neoadjuvant chemoradiotherapy have a poor prognosis that is not improved by surgical resection.<sup>7</sup> In view of the above, the optimal time to identify mediastinal lymph node involvement is before a treatment plan is made rather than intraoperatively or postoperatively. The most recent report of using trimodality in the neoadjuvant setting was by Suntharalingam and colleagues<sup>10</sup> in 2012. Radiation Therapy Oncology Group (RTOG) 0229 was a prospective phase 2 study that looked for the effect of neoadjuvant chemoradiation on mediastinal lymph nodes, survival, and patterns of recurrence. Using weekly carboplatin/paclitaxel and concurrent radiotherapy 61.2 Gy, mediastinal nodal clearance was accomplished in 63% with relatively minimal morbidity and only one postoperative grade 5 toxicity.

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